Studies on the Analgesic Action of Adrenergic Amines

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coarse one. The writer investigated this problem at the statistico-physiological point of view. The main points of this investigation are as follows:

(1) By sprinkling method the lethal effect of silicon carbide powder of different particle sizes to adults of the azuki bean weevil, *Callosobruchus chinensis* L., is investigated under the constant condition of 30° C and 73 %, 91 % and 100 % rerative humidities.

(2) For all particle size, the time-mortality curves prove to be more linear when the net percentage of mortality in probits is plotted against the time of survival after treatment than when it is plotted against the logarithms of time.

(3) Relation between survival time after treatment T and logarithms of particle size d ($\log D \times 10^{-3}$, here D is the diameter of particle) at the 50 percent mortality is represented by the equation, $T + b_2 d = a_2$. And male is more susceptible to lethal effect of silicon carbide than female. The results are summerized in the following table.

Relative humidity	Sex	Regression equation $T + b_2 d = a_2$	Precision of parameters a_2 and b_2 S^2	$V(a_2)$		$V(b_2)$
73%	Female	$T - 2.50881d = 2.86529$	0.04460	0.00558	being	0.04053
	Male	$T - 2.13111d = 1.71258$	0.03489	0.00436	$\bar{d} = 1.27747$	0.03171
91%	Female	$T - 3.38286d = 2.25424$	0.02364	0.00296	being	0.02148
	Male	$T - 3.07448d = 1.57379$	0.06485	0.00811	$\bar{d} = 1.27747$	0.05894
100%	Female	$T - 3.62121d = 1.85541$	0.02113	0.00264	being	0.01920
	Male	$T - 3.52905d = 0.91860$	0.04176	0.00574	$\bar{d} = 1.27747$	0.04176

14. Studies on the Analgesic Action of Adrenergic Amines

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It has been reported that adrenaline, as well as some other adrenergic agents, exerts an analgesic effect, but the experimental evidence in this problem is not yet sufficient. It was intended therefore to study the analgesic activity of the following preparations and to establish the mode of action of adrenergic agents.

I. l-Adrenaline (l-Epinephrine HCl)

II. l-Ephedrine (l-Ephedrine HCl)

III. dl-Methylephedrine (dl-N-methylephedrine HCl)

IV. d-Methylpropamine (d-Desoxyephedrine HCl)

V. d-,dl-, and l-Dimethylpropamine (Desoxymethylephedrine HCl)

VI. d-, dl-, and l-Isolan (3,4-Methylendioxyphenylisopropylamine HCl)

VII. dl-Orthoxine (dl-O-Methoxyphenyl-N-methylisopropylamine HCl)

VIII. l-Nethamine (l-N-Ethylephedrine HCl)

IX. dl-Vonedrine (dl-β-phenyl-n-propylmethylamine HCl)

X. dl-Clopan (dl-Cyclopentyl-isopropylmethylamine HCl)

Results obtained are as follows:

(1) More or less analgesic activity of all these preparations was ascertained by means of the Haffner Method in mice, and by the modification of the Hardy Wolff radiant heat technique in human subjects.

(2) Among the above mentioned preparations d-form (optic isomeride) of IV, V and VI produced very marked analgesia in human subjects and in mice, while the l-form of these preparations showed only a weak effect (Fig. 1). At the same

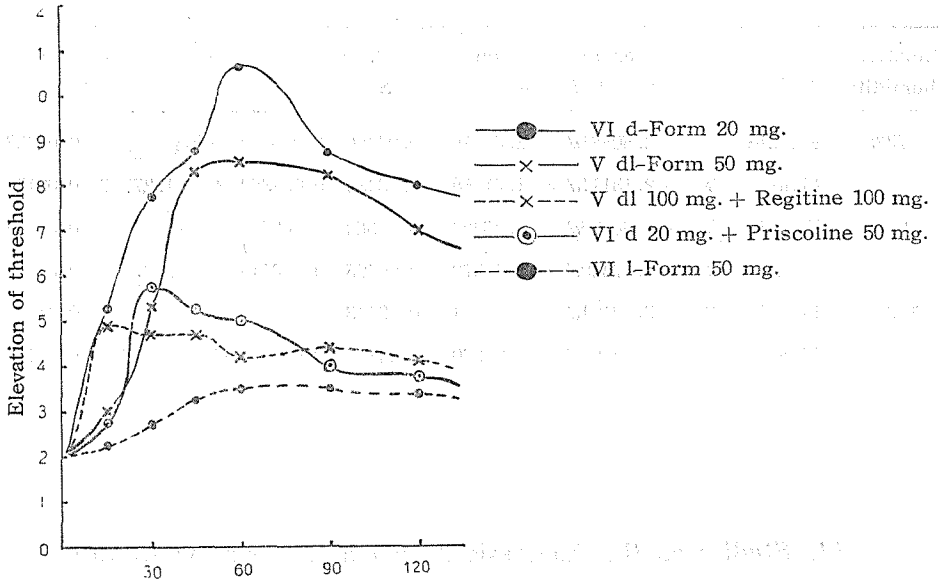

Fig. 1. The curves represent average of the pain threshold for 6 human subjects (cross-over test) by radiant heat method.

time d-preparations caused far stronger stimulant action on CNS (Central nerve system) than l-preparations, as if the analgesic activity of these drugs runs parallel to the CNS stimulating effect. Preparation VII, VIII, IX and X, however, also showed moderate analgesic action, in spite of the slight stimulatory action on CNS.

(3) Either d- or l-form of the preparation IV, V and VI produced a similar antagonistic action against the hypnotic effect of evipan as indicated in Table 1.

(4) When the adrenolytic agent——Regitine (2-[N-p'-tolyl-N-(m'-hydroxyphenyl)-aminomethyl]-imidazoline HCl) and Priscoline (2-Benzyl-imidazoline HCl)—— was

applied combining with any of the above drugs the analgesic activity of them was markedly reduced (*Fig. 1*).

Table 1. The antagonistic effects of the optical isomerides of adrenergic amines against Evipan in mice.

Drug		Mean waking time (minutes) the limits of P = 0.95
Evipan Na (=E)*		47 (37.21 — 57.81)
VI** + E	d-Form	20 (11.90 — 33.60)
	l-Form	22 (11.60 — 41.80)
V** + E	d-Form	32 (13.40 — 52.80)
	l-Form	32 (20.00 — 51.20)
IV** + E	d-Form	18 (11.92 — 27.18)

* Evipan: 0.5mg./10g. i.P. **IV, V and VI: 0.15mg./10g. i.P.

15. Changes of Chemical Constituents of Barley during Malting

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In the previous paper (This Bulletin, **31**, 232 (1953)), it was found that ammonium phosphate added to steep liquor produced a favorable effect on barley malting in accelerating the formation of amylases and in lowering the consumption of starch of green malts.

In the present paper, changes of chemical constituents (nitrogen matters, sugars and soluble phosphorus) of barley during malting were observed with barley (Siga Zairai) steeped in *0.1 M* ammonium phosphate (B) or in water (A). Process of malting was carried out in the same manner as was mentioned in the previous paper.

I. Changes of nitrogen matters.

Hordein- and glutelin-nitrogens decreased gradually during germination, while salt (K_2SO_4)-soluble nitrogen increased rapidly, as was already mentioned. However, hordein nitrogen of the malt (B) steeped in ammonium phosphate increased at first (during 1~3 days' germination) and then gradually decreased.

Albumin-, globulin- and amino-nitrogens always increased during germination, especially amino-nitrogen attained to the amount of thirty times of that (2 mg. N/1000 corns) of original barley. Albumin- and amino-nitrogens of the malt (B) were found to be higher than those of ordinary malt (A).